Component 3

Pharmacologic Therapy

Managing the Child with Asthma:
Component 3 – Pharmacologic Therapy

A stepwise approach to treating the child with asthma is recommended to gain and maintain control of asthma.

- The amount and frequency of medication is dictated by asthma severity and directed toward suppression of airway inflammation.
- Initiate therapy, taking into consideration the needs and circumstances of the child and the child's family.

There are 2 approaches to gaining control of asthma. The first approach is generally preferred because it achieves rapid control.

1. Start with aggressive therapy to achieve rapid control and then step down to the minimum therapy needed to maintain control. Aggressive therapy is therapy at a higher level than corresponds to the initial evaluation of the child's asthma severity. It may be accomplished either by adding a 3- to 10-day course of oral corticosteroids to inhaled corticosteroids, cromolyn, or nedocromil, or by using a higher dose of inhaled corticosteroids.

OR

2. Start with therapy that corresponds to the initial evaluation of the child's asthma severity and step up therapy until control is achieved and maintained.

- Step down therapy gradually when control is achieved (see page 78).
- Monitor continually to ensure that control is maintained at the lowest possible level with minimal adverse effects.
- Choose medications and delivery devices according to the child's ability to use them.
- Consider consulting an asthma specialist for infants and young children who require daily (long-term control) medications, and for children who received more than 2 bursts of oral corticosteroids in the prior 12 months.

The aim is to gain control promptly and "step down" to the minimum therapy needed to maintain control.

What medications are used to treat children with asthma?

	Long-term Control Medications	Quick-relief Medications
Take:	• Daily and chronically (for long periods of time) to maintain control of persistent asthma and to prevent exacerbations	• To treat acute symptoms (coughing, wheezing, difficulty breathing, chest tightness) and to prevent exercise-induced bronchospasm
Include:	• Cromolyn sodium • Inhaled corticosteroids • Oral corticosteroids • Leukotriene modifiers • Long-acting beta$_2$-agonists • Nedocromil sodium • Sustained-release theophylline	• Short-acting inhaled or oral beta$_2$-agonists • Oral corticosteroids (short course) • Ipratropium bromide

See pages 66-69 for recommendations on how to use these medications for treating children with different levels of asthma severity.

Medications to Treat Asthma in Children

LONG-TERM CONTROL MEDICATIONS are taken daily on a long-term basis to achieve and maintain control of persistent asthma.

- Cromolyn sodium
- Nedocromil sodium
- Oral corticosteroids
- Inhaled corticosteroids
- Leukotriene modifiers
- Long-acting beta$_2$-agonists
- Sustained-release theophylline

Cromolyn sodium/Nedocromil sodium

- Inhaled anti-inflammatory agents.
- Available as metered-dose inhaler (MDI). Cromolyn sodium is also available as nebulizer solution.
- Alternative therapy to low-doses of inhaled corticosteroids in mild persistent asthma.
- Nedocromil may also be added to inhaled corticosteroids in moderate asthma.
- Can be used to prevent symptoms to anticipated exposures (cold air, exercise, allergens) on an as-needed basis.
- Improve symptoms and pulmonary function.
- Reduce the need for quick-relief medications.
- Good safety profiles.
- For some children, nedocromil sodium has an unpleasant taste.

Inhaled corticosteroids

- Most potent and effective long-term anti-inflammatory medications currently available.
- Available as MDI and dry powder inhaler (DPI).
- Used for management of persistent asthma at all levels of severity.
- Broad action on inflammatory processes.
- Improve symptoms and pulmonary function.
- Reduce the need for quick-relief medications.
- Fewer side effects than oral corticosteroids.
- Some studies of inhaled corticosteroids to treat asthma in prepubertal children have identified growth delay or suppression that appears to be dose-dependent; others have not. The potential small risk of adverse effects on linear growth is well balanced by efficacy. The clinical significance of the findings is unclear. Monitoring growth is recommended.
- Spacer/holding chamber devices with MDIs and mouth washing after inhalation decrease local side effects and systemic absorption from the gastrointestinal tract.

Oral corticosteroids

- Broad anti-inflammatory effects.
- Long-term use is associated with systemic effects.

  ⇒ Use lowest possible dose and/or alternate day dosing in severe persistent asthma.

Leukotriene modifiers

- Leukotriene receptor antagonists (e.g., montelukast*, zafirlukast) block LTD_4 receptors; 5-lipoxygenase inhibitors (e.g., zileuton) block synthesis of all leukotrienes.
- Available as tablets.
- May be considered as alternative therapy to low doses of inhaled corticosteroids for children with mild persistent asthma, but the position of leukotriene modifiers in therapy has not been fully established. Some studies suggest that leukotriene modifiers may be effective when added to inhaled corticosteroids in the management of moderate persistent asthma (step 3) and when given the night before exercise to prevent exercise-induced brochospasm.
- Improve symptoms and pulmonary function.
- Reduce the need for quick-relief medications.
- Elevations of liver enzymes have been reported with zileuton in some patients. Monitoring is recommended.
- In rare cases, adult patients have presented with systemic eosinophilia and vasculitis with clinical features consistent with Churg Strauss syndrome. These events usually have been associated with reducing oral corticosteroid therapy while initiating a leukotriene modifier therapy. No causal relationship has been established.

* Available since publication of the EPR-2.

Long-acting beta$_2$-agonists

- Relax bronchial smooth muscle.
- Add-on therapy to inhaled corticosteroids for long-term control of symptoms, especially nighttime symptoms.
- Improve symptoms and reduce need for quick-relief medication.
- Available as MDI, DPI, and tablets. Inhaled route of administration is preferred.
- Slower onset and longer duration of action than short-acting beta$_2$-agonists.

- **DO NOT REPLACE ANTI-INFLAMMATORY MEDICATIONS.**
- **Should not be used to treat acute symptoms or exacerbations.**

- Prevent exercise-induced bronchospasm. However, in some patients a diminished brochoprotective effect may be observed when used daily as continuous therapy. The clinical significance of this finding is unclear.
- May produce more effective symptom control when added to standard doses of inhaled corticosteroids compared to increasing the corticosteroid dose alone.

Methylxanthines (theophylline)

- Produce mild to moderate bronchodilation.
- Add-on therapy to anti-inflammatory medications for long-term control of symptoms, especially nighttime symptoms.
  ⇒ Theophylline is an alternative, but not preferred, therapy for persistent asthma.
- Available as tablets and capsules.
- Monitoring is required to maintain serum levels between 5 and 15 mcg/mL.
- Febrile viral illnesses, age, certain medications (e.g., erythromycin), and diet can increase absorption and bioavailability, thereby increasing serum levels.
- Adverse effects include nausea, insomnia, hyperactivity. Seizures can occur if recommended serum levels are exceeded.
- Side effects increase with increasing serum levels. In some children side effects may occur with low serum levels.

QUICK-RELIEF MEDICATIONS give prompt relief of bronchoconstriction and accompanying acute symptoms: coughing, wheezing, shortness of breath or rapid breathing, chest tightness.

- Short-acting beta$_2$-agonists
- Oral corticosteroids
- Anticholinergics

Short-acting beta$_2$-agonists

- Relax bronchial smooth muscle, resulting in bronchodilation usually within 5 to 10 minutes of administration.
- Therapy of choice for relieving acute symptoms and preventing exercise-induced bronchospasm.
- Overuse indicates a need to evaluate and possibly increase (or start) long-term control therapy.

Oral corticosteroids

- Broad anti-inflammatory effects.
- Use a short (3- to 10-day) course to gain initial control of asthma and to speed resolution of moderate persistent or severe persistent exacerbations.

  ⇒ A course of 7 days or less is usually sufficient. In some cases, the exacerbation requires up to 10 days of treatment.
- Tapering dose is not necessary.

Anticholinergics (ipratropium bromide)

- Possible additive benefit to inhaled beta$_2$-agonists for severe exacerbations.
- Possible alternative bronchodilator for children who do not tolerate inhaled beta$_2$-agonists.

Medications expected to become available soon in the U.S.

Further studies and clinical experience will help determine the position these medications will have in asthma therapy.

Long-term control medications

- Mometasone furoate dry powder inhaler (inhaled corticosteroid with dry powder delivery).
- Budesonide nebulizing suspension (inhaled corticosteroid for nebulizer delivery).

Stepwise Approach for Managing Asthma in Infants and Young Children (≤ 5 Years of Age) with Acute or Chronic Asthma Symptoms

	Long-Term Control	Quick-Relief
step 4 Severe Persistent	Daily anti-inflammatory medications: • High-dose inhaled corticosteroid with spacer/holding chamber and face mask. AND • If needed, add systemic corticosteroids 0.25 - 2 mg/kg/day and reduce to lowest daily or alternate-day dose that stabilizes symptoms.	• Short-acting bronchodilator as needed for symptoms. Intensity of treatment depends on severity of exacerbation. • Either: ⇒ Inhaled short-acting beta$_2$-agonist by nebulizer or spacer/holding chamber and face mask. OR ⇒ Oral beta$_2$-agonist. **Daily or increasing use of short-acting, inhaled beta$_2$-agonists may indicate need for additional long-term control therapy.***
step 3 Moderate Persistent	Daily anti-inflammatory medications. Either: • Medium-dose inhaled corticosteroid with spacer/holding chamber and face mask. OR, once control is established, • Low to medium-dose inhaled corticosteroid and nedocromil. OR • Low to medium-dose inhaled corticosteroid and long-acting bronchodilator (theophylline).	• Short-acting bronchodilator as needed for symptoms. Intensity of treatment depends on severity of exacerbation. • Either: ⇒ Inhaled short-acting beta$_2$-agonist by nebulizer or spacer/holding chamber and face mask. OR ⇒ Oral beta$_2$-agonist. **Daily or increasing use of short-acting, inhaled beta$_2$-agonists may indicate need for additional long-term control therapy.***
step 2 Mild Persistent	Daily anti-inflammatory medication. Either: • Cromolyn (nebulizer preferred, or MDI) or nedocromil (MDI) tid-qid. Infants and young children usually begin with a trial of cromolyn or nedocromil. OR • Low-dose inhaled corticosteroid with spacer/holding chamber and face mask.	• Short-acting bronchodilator as needed for symptoms. Intensity of treatment depends on severity of exacerbation. • Either: ⇒ Inhaled short-acting beta$_2$-agonist by nebulizer or spacer/holding chamber and face mask. OR ⇒ Oral beta$_2$-agonist. **Daily or increasing use of short-acting, inhaled beta$_2$-agonists may indicate need for additional long-term control therapy.***
step 1 Mild Intermittent	• No daily medication.	• Short-acting bronchodilator as needed for symptoms < 2x/wk. Intensity of treatment depends on severity of exacerbation. • Either: ⇒ Inhaled short-acting beta$_2$-agonist by nebulizer or spacer/holding chamber and face mask. OR ⇒ Oral beta$_2$-agonist. **Daily or increasing use of short-acting, inhaled beta$_2$-agonists may indicate need for additional long-term control therapy.***

Step Down	* Step Up
Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible.	If control is not maintained, consider stepping up. First, review patient medication technique, adherence, and environmental control (avoidance of allergens and/or other factors that contribute to asthma severity).

For exacerbations triggered by viral upper respiratory infections, use short-acting bronchodilator q4-6 hr, as needed, up to 24 hr (longer with physician consult).

- If exacerbations occur more frequently than every 6 weeks, consider starting or increasing the dose of anti-inflammatory long-term control therapy (step 2 or 3).
- Consider 3- to 10-days of systemic corticosteroids:
  ⇒ If the exacerbation is severe.
  ⇒ At the onset of a viral respiratory infection in a child with a history of previous severe exacerbations.

The stepwise approach presents guidelines to assist clinical decision-making. Asthma is highly variable. Clinicians should tailor specific medication plans to the needs and circumstances of the child and family.

- Gain control as quickly as possible. Start treatment with either:
  ⇒ Aggressive therapy (e.g., a course of systemic corticosteroids added to the therapy that corresponds to the child's initial level of severity); OR
  ⇒ The step that corresponds to the child's initial severity, and step up if necessary.

THEN gradually decrease treatment to the least medication necessary to maintain control.

- A rescue course of systemic corticosteroid may be needed at any time and step.
- In general, increasing use of a short-acting beta$_2$-agonist or use on a daily basis indicates the need for additional long-term control therapy.
- Some children with intermittent asthma experience severe and life-threatening exacerbations separated by long periods of normal lung function and no symptoms. This may be especially common with exacerbations provoked by respiratory infections. A short course of systemic corticosteroids is recommended.
- At each step, children and their parents should control their environment to avoid or control factors that make their asthma worse (e.g., allergens, irritants). This requires specific diagnosis and patient education.
- Consultation with an asthma specialist is *recommended* for children with moderate or severe persistent asthma in this age group. Consultation should be considered for all children with mild persistent asthma.
- It is important to remember that there are very few studies on asthma therapy for infants.

Goals of therapy:

- Minimal (ideally NO) symptoms during the day or at night
- Minimal (ideally NO) asthma episodes
- Minimal use (< 1x/day) of short-acting beta$_2$-agonist
- PEF ≥ 80% of personal best, if used
- Minimal (ideally NO) adverse effects from medications
- NORMAL ACTIVITIES

Maintain the child on the lowest dose of medication that controls asthma.

To keep medications at a minimum, use environmental control measures for:

- Tobacco and/or wood smoke
- Allergens to which the child is sensitive (e.g., dust mites, cockroaches, molds, animal dander)
- Other airborne irritants (e.g., fumes, odors)

Stepwise Approach for Managing Asthma in Children > 5 Years of Age with Acute or Chronic Asthma Symptoms

	Long-Term Control	Quick-relief
step 4 Severe Persistent	Daily medications: • Anti-inflammatory: high-dose inhaled corticosteroid. AND • Long-acting bronchodilator (e.g., either long-acting, inhaled beta$_2$-agonist or sustained-release theophylline). AND • Corticosteroid tablets or syrup long-term (2 mg/kg/day, generally not to exceed 60 mg per day); make repeated attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.	• Short-acting bronchodilator: inhaled beta$_2$-agonist as needed for symptoms. Intensity of treatment depends on severity of exacerbation. **Daily or increasing use of short-acting, inhaled beta$_2$-agonists may indicate need for additional long-term control therapy.***
step 3 Moderate Persistent	Daily medication: • Anti-inflammatory: either medium-dose inhaled corticosteroid. OR • Low- to medium-dose inhaled corticosteroid and add a long-acting bronchodilator, especially for nighttime symptoms (e.g., either long-acting, inhaled beta$_2$-agonist or sustained-release theophylline). • If needed, medium- to high-dose inhaled corticosteroid and long-acting bronchodilator, especially for nighttime symptoms.	• Short-acting bronchodilator: inhaled beta$_2$-agonist as needed for symptoms. Intensity of treatment depends on severity of exacerbation. **Daily or increasing use of short-acting, inhaled beta$_2$-agonists may indicate need for additional long-term control therapy.***
step 2 Mild Persistent	One daily medication: • Anti-inflammatory: EITHER ⇒ Low-dose inhaled corticosteroid OR ⇒ Cromolyn or nedocromil (children usually begin with a trial of cromolyn or nedocromil). • Sustained-release theophylline (to serum concentration of 5-15 mcg/mL) is an alternative, but not preferred, therapy. • A leukotriene modifier may be considered although their position in therapy is not fully established.	• Short-acting bronchodilator: inhaled beta$_2$-agonist as needed for symptoms. Intensity of treatment depends on severity of exacerbation. **Daily or increasing use of short-acting, inhaled beta$_2$-agonists may indicate need for additional long-term control therapy.***
step 1 Mild Intermittent	• No daily medication needed.	• Short-acting bronchodilator: inhaled beta$_2$-agonist as needed for symptoms. Intensity of treatment depends on severity of exacerbation. **Daily or increasing use of short-acting, inhaled beta$_2$-agonists may indicate need for additional long-term control therapy.***

Step Down	* Step Up
Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible.	If control is not maintained, consider stepping up. First, review patient medication technique, adherence, and environmental control (avoidance of allergens and/or other factors that contribute to asthma severity).

For exacerbations triggered by viral upper respiratory infections, use short-acting bronchodilator q4-6 hr, as needed, up to 24 hr (longer with physician consult).

- If exacerbations occur more frequently than every 6 weeks, consider starting or increasing the dose of anti-inflammatory long-term control therapy (step 2 or 3).
- Consider 3-10 days of systemic corticosteroids
  - ⇒ If the exacerbation is severe.
  - ⇒ At the onset of a viral respiratory infection in a child with a history of previous severe exacerbations.

The stepwise approach presents guidelines to assist clinical decision-making. Asthma is highly variable. Clinicians should tailor specific medication plans to the needs and circumstances of the child and family.

- Gain control as quickly as possible. Start treatment with either:
  - ⇒ Aggressive therapy (e.g., a course of systemic corticosteroids added to the therapy that corresponds to the child's initial level of severity); OR
  - ⇒ The step that corresponds to the child's initial severity, and step up if necessary.

THEN gradually decrease treatment to the least medication necessary to maintain control.

- A rescue course of systemic corticosteroid may be needed at any time and step.
- In general, increasing use of a short-acting beta$_2$-agonist or use on a daily basis indicates the need for additional long-term control therapy.
- Some children with intermittent asthma experience severe and life-threatening exacerbations separated by long periods of normal lung function and no symptoms. This may be especially common with exacerbations provoked by respiratory infections. A short course of systemic corticosteroids is recommended.
- At each step, children and their parents should control their environment to avoid or control factors that make their asthma worse (e.g., allergens, irritants). This requires specific diagnosis and patient education.
- Referral to an asthma specialist for consultation or co-management is *recommended* if there are difficulties achieving or maintaining control of asthma or if the child requires step 4 care. Referral may be *considered* if the child requires step 3 care.

Goals of therapy:

- Minimal (ideally NO) symptoms during the day or at night
- Minimal (ideally NO) asthma episodes
- Minimal use (< 1x/day) of short-acting beta$_2$-agonist
- PEF ≥ 80% of personal best, if used
- Minimal (ideally NO) adverse effects from medications
- NORMAL ACTIVITIES

Maintain the child on the lowest dose of medication that controls asthma.

To keep medications at a minimum, use environmental control measures for:

- Tobacco and/or wood smoke
- Allergens to which the child is sensitive (e.g., dust mites, cockroaches, molds, animal dander)
- Other airborne irritants (e.g., fumes, odors)

Medications to Treat Children with Asthma in the United States

The most important determinant of appropriate dosing is the clinician's judgment of the child's response to therapy. The clinician must monitor several clinical parameters to assess both efficacy and adverse effect, and adjust the dose accordingly.

The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control.

Long-Term Control Medications

Cromolyn sodium/Nedocromil sodium

Generic name	Brand name(s)	Dosage form(s)	Dose[1]	Potential adverse effects and therapeutic issues
Cromolyn sodium	Intal®	MDI: 1 mg/puff Nebulizer solution: 20 mg/2 mL ampule (unit dose[2,3])	1-2 puffs, t.i.d.-q.i.d. 1 ampule, t.i.d.-q.i.d.	• Therapeutic response to cromolyn and nedocromil often occurs within 2 weeks, but a 4- to 6-week trial may be needed to determine maximum benefit. • Dose of cromolyn MDI (1 mg/puff) may be inadequate to affect airway hyperresponsiveness. Nebulizer delivery (20 mg/ampule) may be preferred for some patients. • Safety is the primary advantage of these agents.
Nedocromil sodium	Tilade®	MDI: 1.75 mg/puff	1-2 puffs, b.i.d.-q.i.d.	• Unpleasant taste for some patients.

[1]These doses are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs of the child and family.
[2]Do not use partial unit dose.
[3]Some nebulizer solutions contain benzalkonium which may cause broncospasm in some patients.

Long-Term Control Medications

Inhaled corticosteroids

Generic name	Brand name(s)	Dosage form(s)	Dose[1]			Potential adverse effects and therapeutic issues
			low	medium	high	
Beclomethasone dipropionate	Beclovent®, Vanceril®	MDI: 42 mcg/puff	2-8 puffs/day	8-16 puffs/day	> 16 puffs/day	**FOR ALL INHALED CORTICOSTEROIDS:** • Cough, dysphonia, candidiasis; high-doses may have systemic effects although studies are not conclusive and clinical significance is not clear. Monitoring growth is recommended. • The potential risks of inhaled corticosteroids are well balanced by their benefits. • To minimize local and systemic adverse effects, titrate to lowest effective dose and, if using MDIs, use MDI with a spacer/holder chamber.
	Vanceril-DS®	MDI: 84 mcg/puff	1-4 puffs/day	4-8 puffs/day	> 8 puffs/day	
Budesonide	Pulmicort Turbuhaler®	DPI: 200 mcg/puff	1 puff/day	1-2 puffs/day	> 2 puffs/day	
Flunisolide	AeroBid®, AeroBid®-M	MDI: 250 mcg/puff	2-3 puffs/day	4-5 puffs/day	> 5 puffs/day	
Fluticasone propionate	Flovent®	MDI: 44 mcg/puff 110 mcg/puff 220 mcg/puff DPI: 50 mcg/puff 100 mcg/puff 250 mcg/puff	2-4 puffs/day — — 2-4 puffs/day — —	4-10 puffs/day 2-4 puffs/day — 4-10 puffs/day 2-4 puffs/day —	> 10 puffs/day > 4 puffs/day > 2 puffs/day > 10 puffs/day > 4 puffs/day > 2 puffs/day	
Triamcinolone	Azmacort®	MDI: 100 mcg/puff	4-8 puffs/day	8-12 puffs/day	> 12 puffs/day	

[1]These doses are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs of the child and family.

Long-Term Control Medications

Oral corticosteroids

Generic name	Brand name(s)	Dosage form(s)	Dose[1]	Potential adverse effects and therapeutic issues
Methylprednisolone	Medrol®	Tablet: 2, 4, 6, 8, 16, 32 mg	• 0.25-2 mg/kg daily in single dose or q.i.d. as needed for control • Short-course (3- to 10-day) "burst:" 1-2 mg/kg/day (max: 60 mg/day)	**FOR ALL ORAL STEROIDS:** • Long-term use is associated with systemic effects. Use at lowest effective dose either daily or on alternate days (which may lessen adrenal suppression). • Short courses or "bursts" are effective for establishing control when initiating therapy or during a period of gradual deterioration. • Short-term therapy should continue until child achieves 80% PEF personal best, or until symptoms resolve (usually within 3- to 10-days, but may take longer). There is no evidence that tapering the dose following improvement prevents relapse.
Prednisolone	Prelone® Pediapred®	Tablet: 5 mg Liquid: 15 mg/5 mL; Liquid: 5 mg/5 mL	• 0.25-2 mg/kg daily in single dose or q.i.d. as needed for control • Short-course (3- to 10-day) "burst," 1-2 mg/kg/day (max: 60 mg/day)	
Prednisone	Prednisone Deltasone® Prednisone Intensol™	Tablet: 1, 2.5, 5, 10, 20, 25 mg Liquid: 5 mg/mL	• 0.25-2 mg/kg daily in single dose or q.i.d. as needed for control • Short-course (3- to 10-day) "burst," 1-2 mg/kg/day (max: 60 mg/day)	

[1]These doses are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs and circumstances of the child and family.

Long-Term Control Medications

Leukotriene modifiers

Generic name	Brand name(s)	Dosage form(s)	Dose[1]	Potential adverse effects and therapeutic issues
Montelukast	Singulair®	Tablet: 5 mg, chewable, for ages 6-14 yrs; 10 mg, for ages > 14 yrs	1 tablet in evening	• Data about adverse effects in patients are limited. Increased clinical experience and further study in a wide range of patients are needed to determine those children most likely to benefit from leukotriene modifiers and to establish a more specific role for these medications in asthma therapy.
Zafirlukast	Accolate®	Tablet: 20 mg, for ages ≥ 12 yrs; 10 mg, for ages 7-11 yrs.	1 tablet b.i.d. Take 1 hour before or 2 hours after meals	• Data about adverse effects in patients are limited. Increased clinical experience and further study in a wide range of patients are needed to determine those children most likely to benefit from leukotriene modifiers and to establish a more specific role for these medications in asthma therapy. • Drug interactions: warfarin increases prothrombin time.
Zileuton	Zyflo™ Filmtab®	Tablet: 600 mg, for ages ≥ 12 yrs	1 tablet q.i.d.	• Data about adverse effects in patients are limited. Increased clinical experience and further study in a wide range of patients are needed to determine those children most likely to benefit from leukotriene modifiers and to establish a more specific role for these medications in asthma therapy. • Drug interactions: terfenadine, warfarin, theophylline • Possible elevation of liver enzymes requires monitoring.

[1]These doses are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs of the child and family.

Long-Term Control Medications

Long-acting beta$_2$-agonists

Generic name	Brand name(s)	Dosage form(s)	Dose[1]	Potential adverse effects and therapeutic issues
Salmeterol	Serevent® Serevent® Diskus®	MDI: 21 mcg/puff DPI: 50 mcg/blister	1-2 puffs, b.i.d. 1 puff, b.i.d.	• Tachycardia, tremor. The clinical relevance of potential diminished bronchoprotective effect is uncertain. • DO NOT USE in place of anti-inflammatory therapy.
Sustained-release albuterol	Volmax®, Proventil Repetabs®	Tablet: 4 mg	Maximal dose: 6-12 yr: 4 mg b.i.d. ≥12 yr: 8 mg b.i.d.	• Tachycardia, temor, irritability.

[1]These doses are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs of the child and family.

Methylxanthines

Generic name	Brand name(s)	Dosage form(s)	Dose[1]	Potential adverse effects and therapeutic issues
Theophylline	Aerolate®-III, Aerolate®-JR, Aerolate®-SR, Choledyl®-SA, Slo-bid™, Slo-Phyllin®, Theolair™, Theolair™-SR, T-Phyl®, Uni-Dur®, Uniphyl®	Capsules, tablets	Starting dose: 10 mg/kg/day Maximal dose: < 1 yr old: (0.2 x age in wks) + 5 = mg/kg/day Maximal dose: ≥ 1 yr old: 16 mg/kg/day, not to exceed the adult maximum (800 mg/day)	• Monitoring serum levels (5-15 mcg/mL) is essential to ensure therapeutic, but not toxic, doses are achieved. • Serum levels may be affected by numerous factors (diet, febrile illness, other medications). • Tachycardia, tremor, naseua, vomiting, headache, CNS stimulation.

[1]These doses are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs of the child and family.

Quick-Relief Medications

Short-acting, inhaled beta$_2$-agonists

Generic name	Brand name(s)	Dosage form(s)	Dose[1]	Potential adverse effects and therapeutic issues
Albuterol	Airet™	Nebulizer solution: 2.5 mg/3mL; 0.083% (unit dose[2,3])	0.05 mg/kg (min: 1.25 mg; max: 2.5 mg) t.i.d.-q.i.d.	**FOR ALL SHORT-ACTING BETA$_2$-AGONISTS:** • Tremor, tachycardia, headache
	Proventil® Ventolin®	MDI: 90 mcg/puff	2 puffs, 15 min before exercise; 2 puffs t.i.d.-q.i.d., prn	
	Proventil® Ventolin®	Nebulizer solution: 5 mg/mL (0.5%); 0.083% (unit dose[2,3]) containing 2.5 mg	0.05 mg/kg (min: 1.25 mg; max: 2.5 mg) t.i.d.-q.i.d.	**NOTE:** Increasing use of short-acting beta$_2$-agonists, use of > 1 canister/month, or lack of expected effect, indicates inadequate asthma control. See doctor to increase or add long-term control medication.
	Proventil®-HFA	MDI: 90 mcg/puff	2 puffs t.i.d.-q.i.d., prn	
	Ventolin® Rotacaps	DPI: 200 mcg/capsule	1 capsule, 15 min before exercise; 1 capsule t.i.d.-q.i.d., prn	
Bitolterol	Tornalate®	MDI[4]: 370 mcg/puff	2 puffs t.i.d.-q.i.d., prn	
Levalbuterol	Xopenex®	Nebulizer solution: Unit dose vials[2,3]: 0.63 mg/3 mL 1.25 mg/3 mL	0.63 mg t.i.d. for maintenance 1.25 mg t.i.d. for acute bronchospasm and for patients unresponsive to lower dose	Newly available single isomer of albuterol. Further clinical studies will help establish its role in therapy.
Pirbuterol	Maxair™ Maxair™ Autohaler™	MDI: 200 mcg/puff	2 puffs t.i.d.-q.i.d., prn	

[1]These doses are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs of the child and family.
[2]Do not use partial unit dose.
[3]Some nebulizer solutions contain benzalkonium, which may cause bronchospasm in some patients.
[4]Also available as a nebulizer solution (2 mg/mL = 0.2%), but a children's dose has not been established.

Quick-Relief Medications

Oral corticosteroids

Generic name	Brand name(s)	Dosage form(s)	Dose[1]	Potential adverse effects and therapeutic issues
Methylprednisolone	Medrol®	Tablet: 2, 4, 6, 8, 16, 32 mg	Short-course (3-10 day) "burst": 1-2 mg/kg/day (max: 60 mg/day[2])	**FOR ALL ORAL CORTICOSTEROIDS:** • Although the onset of action is up to 4-6 hours, oral corticosteroids are important to treat moderate-severe exacerbations because they speed resolution of airflow obstruction and help prevent relapse. • Short courses or "bursts" are effective for establishing control when initiating therapy or during a period of gradual deterioration. • Short-term therapy should continue until child acheives 80% PEF personal best or until symptoms resolve (usually within 3-10 days, but may take longer). There is no evidence that tapering the dose following improvement prevents relapse.
Prednisolone	Prelone® Pediapred®	Tablet: 5 mg Liquid: 15 mg/5 mL Liquid: 5 mg/5 mL	Short-course (3-10 day) "burst": 1-2 mg/kg/day (max: 60 mg/day[2])	
Prednisone	Prednisone Prednisone Intensol™	Tablet: 1, 2.5, 5, 10, 20, 25 mg Liquid 5 mg/mL	Short-course (3-10 day) "burst": 1-2 mg/kg/day (max: 60 mg/day[2])	

[1]These doses are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs of the child and family.
[2]A course of 7 days or less is usually sufficient. In some cases, the exacerbation may require up to 10 days of treatment.

Anticholinergics

Generic name	Brand name(s)	Dosage form(s)	Dose[1]	Potential adverse effects and therapeutic issues
Ipratropium bromide	Atrovent®	MDI: 18 mcg/puff Nebulizer solution: 0.20 mg/mL; 0.02% (unit dose[2,3])	1-2 puffs q.i.d. 1 unit dose q.i.d.	• Dry mouth, increased wheezing in some patients. • May provide additive effect(s) to short-acting beta$_2$-agonist.

[1]These doses are suggested as guides for making clinical decisions. The clinician must use his/her judgment to tailor treatment to the specific needs of the child and family.
[2]Do not use partial unit dose.
[3]Some nebulizer solutions contain benzalkonium which may cause broncospasm in some patients.

Making the Stepwise Approach to Therapy Work

When do you start daily therapy with a long-term control medication?

- Daytime symptoms > 2x/week
- Child awakens at night or in early morning with symptoms > 2x/month
- Increased use of short-acting beta$_2$-agonist (other than for preventing exercise-induced asthma or after a viral respiratory infection):
  - ⇒ > 2x/week for child with intermittent asthma
  - ⇒ Daily or increasing use for child with mild or moderate persistent asthma

What is asthma control in children?

- **No coughing**
- **No shortness of breath or rapid breathing,** wheezing, or chest-tightness
- **No waking up at night** because of asthma symptoms
- **Normal activities**, including play, sports and exercise
- **No episodes** of asthma that require a doctor visit, emergency room visit, or urgent care
- **No absences** from school or activities
- **No missed time from work** for the parent or caregiver
- Normal (or near normal) lung function

Treating the underlying inflammation of the airways is essential for preventing and maintaining control of asthma symptoms.

Children with persistent symptoms need daily therapy with a long-term control medication.

- Children who have asthma symptoms less than 2 times per week may only need to use a short-acting beta$_2$-agonist as needed for symptoms.

Carefully monitor the child's response to therapy.

- If there are no clear benefits, stop treatment and consider alternative therapies and/or diagnoses.

How do you step down long-term control therapy?

Stepping down can be achieved by:

- Lower doses
- Fewer doses
- Using a different medication

- After starting daily long-term control medication, regular follow-up visits (at 1- to 6-month intervals) are essential, to ensure that asthma control is maintained with minimal adverse effects.
  - ⇒ Monitor symptoms, especially nighttime awakenings and activity levels.
  - ⇒ Monitor use of quick-relief medications.
  - ⇒ Monitor pulmonary function, preferably with spirometry.
- If asthma is controlled for 3 to 6 months, then gradually decrease the dose, frequency, or number of medications and re-evaluate in 3 to 6 months.
- Most children with persistent asthma continue to benefit from a daily long-term control medication that suppresses underlying airway inflammation.
  - ⇒ Long-term control medications reduce the need for quick-relief medications and may prevent anticipated symptoms (e.g., from exercise, allergens, cold air).
- Always follow a decrease in therapy with close follow-up in the clinic or by phone.
  - ⇒ The child and parents should monitor asthma symptoms and PEF and alert the doctor promptly if worsening occurs.

Maintain the child on the lowest dose of medication that controls asthma.

To keep medications to a minimum, use environmental control measures if the child is sensitive to dust mites, tobacco and/or wood smoke, animal dander, molds, cockroach allergens.

Reduce therapy gradually.

How much to reduce therapy is based on evaluation of the child's asthma severity and any special considerations.

- Asthma can deteriorate at a highly variable rate and intensity.
- For inhaled corticosteroids, some physicians suggest decreasing the dose by 25% every 2-3 months to the lowest possible dose to maintain control.
- Carefully follow up.